IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Box Patent Application
Assistant Commissioner For Patents
Washington, D.C. 20231

NEW APPLICATION TRANSMITTAL

Transmitted herewith for filing is the patent application of James R. Prudent, Jeff G. Hall, Victor Lyamichev, Mary Ann Brow and James B. Dahlberg for **Nucleic Acid Detection Assays.**

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this New Application Transmittal and the documents referred to as enclosed therein are being deposited with the U.S. Postal Service on this date **February 22, 2002** in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number **EL 837 033 803 US** addressed to: **Box Patent Application,** Assistant Commissioner For Patents, Washington, D.C. 20231.

Mary Ellen Waite

1. **Type Of Application**
   This new application is for a(n)
   ☒ Original (nonprovisional)
   ☒ Continuation.
2. **Benefit Of Prior U.S. Application(s)** (35 U.S.C. §§ 119(e), 120, or 121)
   ☒ The new application being transmitted claims the benefit of prior U.S. application(s) and enclosed are ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.
3. **Papers Enclosed That Are Required For Filing Date Under 37 C.F.R. § 1.53(b) (Regular) or 37 C.F.R. § 1.153 (Design) Application**
   230 Pages of Specification
   7 Pages of Claims
   1 Page of Abstract
   87 Sheets of Informal Drawings
4. **Additional Papers Enclosed**
   ☒ Preliminary Amendment
   ☒ Information Disclosure Statement (37 C.F.R. § 1.98), Form PTO-1449 and Citations
5. **Declaration**
   ☒ Enclosed
   ☒ Executed by inventors.
6. **Inventorship Statement**
   The inventorship for all the claims in this application is:
   ☒ the same
7. **Language**
   ☒ English

8. **Fee Calculation (37 C.F.R. § 1.16)**

☒ Regular application

CLAIMS AS FILED

Number Filed	Number Extra	Rate	Basic Fee - $740.00 (37 C.F.R. § 1.16(a))
Total Claims (37 C.F.R. § 1.16(c))	56 - 20 =	36 x $18.00 =	$648.00
Independent Claims (37 C.F.R. § 1.16(b))	3 - 3 =	0 x $84.00 =	$0.00
Multiple Dependent Claim(s), if any (37 C.F.R. § 1.16(d))		+ $280.00 =	$0.00
			$1,388.00
		Petition to Make Special Filing **Fee Calculation**	**$130.00**

9. **Fee Payment Being Made At This Time**

☒ Enclosed

☒ basic filing fee

Total Fees Enclosed **$1,518.00**

10. **Method of Payment of Fees**

☒ Check in the amount of **$1,518.00**

11. **Authorization To Charge Additional Fees and Credit Overpayment**

☒ The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment to Deposit Account No.: **08-1290. An originally executed duplicate of this transmittal is enclosed for this purpose.**

12. **Power of Attorney by Assignee**

☒ The power appears in the original papers in the prior application.

13. **Return Receipt Postcard**

☒ Enclosed

Dated: February 22, 2002

Mary Ann Brow
Registration No.: 42,363

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415/904-6500

☒ **Incorporation By Reference Of Added Pages**

☒ Plus Added Pages For New Application Transmittal Where Benefit Of Prior U.S. Application(s) Claimed

Number of pages added 1

ADDED PAGES FOR APPLICATION TRANSMITTAL
WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED

14. **Relate Back**

A. **35 U.S.C. § 119(e)**

B. **35 U.S.C. §§ 120, 121 and 365(c)**

☒ Amend the Specification by inserting before the first line the sentence: This is a Continuation of co-pending U.S. Appln. Ser. No. **09/982,667, filed October 18, 2001**, which is a continuation of U.S. Appln. Ser. No. **09/350,309, filed July 9, 1999**, now U.S. Patent No. 6,348,314, which is a Divisional of U.S. Appln. Ser. No. **08/756,386, filed November 29, 1996,** now U.S. Patent No. 5,985,557, which is a Continuation-In-Part of U.S. Appln. Ser. No. **08/682,853, filed July 12, 1996,** now U.S. Patent No. 6,001,567, which is a Continuation-In-Part of U.S. Appln. Ser. No. **08/599,491, filed January 24, 1996,** now U.S. Patent No. 5,846,717.

15. **Further Inventorship Statement Where Benefit Of Prior Application(s) Claimed**

a. This application discloses and claims only subject matter disclosed in the prior application whose particulars are set out above and the inventor(s) in this application are

☒ the same.

#8/IDS1

PATENT
Attorney Docket No. **FORS-06910**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: James R. PRUDENT *et al.*
Serial No.: Group No.:
Filed: Examiner:
Entitled: **INVASIVE CLEAVAGE OF NUCLEIC ACIDS**

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service as "Express Mail Post Office to Addressee" under Express Mail Label No. EL 837 033 803 US in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: February 22, 2002 By: Mary Ellen Waite
Mary Ellen Waite

Sir or Madam:

The citations listed below may be material to the examination of the above-identified application, and are therefore submitted in compliance with the duty of disclosure defined in 37 C.F.R. §§ 1.56 and 1.97. The Examiner is requested to make these citations of official record in this application. Except for five references indicated below, copies of all references were provided in parent U.S. Patent Appln., Ser. No. 09/530, 309, now U.S Patent No. 6,348,314. Copies of the five additional references are attached hereto.

The following printed publications are referred to in the body of the specification:

- U.S. Patent No. 4,511,502;
- U.S. Patent No. 4,511,503;
- U.S. Patent No. 4,512,922;
- U.S. Patent No. 4,518,526;
- U.S. Patent No. 4,683,194;
- U.S. Patent No. 4,683,195;
- U.S. Patent No. 4,683,202;
- U.S. Patent No. 4,775,619;

- U.S. Patent No. 4,876,187;
- U.S. Patent No. 5,011,769;
- U.S. Patent No. 5,108,892;
- U.S. Patent No. 5,118,605;
- U.S. Patent No. 5,144,019;
- U.S. Patent No. 5,210,015;
- U.S. Patent No. 5,403,711;
- U.S. Patent No. 5,422,253;
- U.S. Patent No. 5,427,930;
- U.S. Patent No. 5,494,810;
- PCT International Application No. WO 92/06200;
- PCT International Application No. WO 90/01069 A1;
- PCT International Application No. WO 91/09950;
- PCT International Application No. WO 90/15157 A1;
- EP 0 482 714 A1

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- Bergseid *et al.*, "A High Fidelity Thermostable DNA Polymerase Isolated from *Pyrococcus Furiosus*," *Strategies* 4:34-35 (1991);
- Brow *et al.*, "Differentiation of Bacterial 16S rRNA Genes and Intergenic Regions and *Mycobacterium tuberculosis katG* Genes by Structure-Specific Endonuclease Cleavage," *J. of Clin. Micro.* 34:3129-3137 (1996);
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- Ceska *et al.*, "A helical arch allowing single-stranded DNA to thread through T5 5'-exonuclease," *Nature* 382:90-93 (1996);
- Copley and Boot, "Exonuclease Cycling Assay: An Amplified Assay for the Detection of Specific DNA Sequences," *BioTechniques* 13:888-891 (1992);
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- Harrington and Lieber, "Functional domains within FEN-1 and RAD2 define a family of structure-specific endonucleases: implications for nucleotide excision repair," *Genes and Develop.* 8:1344-1355 (1994);
- Hiraro *et al.* "Most compact hairpin-turn structure exerted by a short DNA fragment, d(GCGAAGC) in solution: an extraordinarily stable structure resistant to nucleases and heat," *Nuc. Acids Res.* 22:576-582 (1994);
- Holland *et al.*, "Detection of specific polymerase chain reaction product by utilizing the 5'-3' exonuclease activity of *Thermus aquaticus* DNA polymerase," *Proc. Natl. Acad. Sci. USA* 88:7276-7280 (1991);
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of Viral RNA in Infected Sera by Polymerase Chain Reaction," *Hepatology* 14:595-600 (1991);

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- Marmur and Lane, "Strand Separation and Specific Recombination in Deoxyribonucleic acids: Biological Studies," *Proc. Natl. Acad. Sci. USA* 46:453-461 (1960);
- Mathur *et al.*, The DNA polymerase gene from the hyperthermophilic marine archaebacterium *Pyrococcus furiosus*, shows sequence homology with α-like DNA polymerases," *Nucl. Acids Res.* 19:6952 (1991);
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- Perler *et al.*, "Intervening sequences in an Archaea DNA polymerase gene," *Proc. Natl. Acad. Sci.* USA 89:5577-5581 (1992);
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- Studier and Moffatt, "Use of Bacteriophage T7 RNA Polymerase to Direct Selective High-level Expression of Cloned Genes," *J. Mol. Biol.* 189:113-130 (1986);
- Tindall and Kunkel, "Fidelity of DNA by the *Thermus aquaticus* DNA Polymerase," *Biochem.* 27:6008-6013 (1998);
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- Wu and Wallace, "The Ligation Amplification Reaction (LAR) - Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," *Genomics* 4:560-569 (1989); and
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Applicants have become aware of the following printed publications that may be material to the examination of this application. A number of these references are not prior art, but are provided for thoroughness. Copies of these references were provided in parent U.S. Patent Appln., Ser. No. 09/530, 309, now U.S Patent No. 6,348,314.

The following references are patents or patent applications assigned to the applicant of the present invention.

- U.S. Patent No. 6,348,314
- U.S. Patent No. 6,214,545
- U.S. Patent No. 6,210,880
- U.S. Patent No. 6,194,149
- U.S. Patent No. 6,001,567
- U.S. Patent No. 5,994,069
- U.S. Patent No. 5,985,557
- U.S. Patent No. 5,846,717
- U.S. Patent No. 5,843,669
- U.S. Patent No. 5,843,654
- U.S. Patent No. 5,837,450
- U.S. Patent No. 5,888,780
- U.S. Patent No. 5,795,763
- U.S. Patent No. 5,719,028
- U.S. Patent No. 5,691,142
- U.S. Patent No. 5,614,402
- U.S. Patent No. 5,541,311
- PCT International Application No. WO 01/98537
- PCT International Application No. WO 01/90337
- PCT International Application No. WO 98/50403
- PCT International Application No. WO 98/42873
- PCT International Application No. WO 98/23774
- PCT International Application No. WO 97/27214
- PCT International Application No. WO 96/15267
- PCT International Application No. WO 94/29482

The following references were cited by Examiners in U.S. prosecution or foreign search

reports for related cases.

- U.S. Patent No. 5,698,400
- U.S. Patent No. 5,660,988
- U.S. Patent No. 5,601,976
- U.S. Patent No. 5,545,729
- U.S. Patent No. 5,487,972
- U.S. Patent No. 5,407,795
- U.S. Patent No. 5,380,833
- U.S. Patent No. 4,818,680
- Agrawal *et al.,* "Modified oligonucleotides as therapeutic and diagnostic agents," *Current Opinion in Biotechnology*, 6:12-19 (1995);
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- Gamper *et al.,* "Solution Hybridization of Crosslinkable DNA Oligonucleotides to Bacteriophage M13 DNA," *J. Mol. Biol.* 197:349-362 (1987);
- Lima *et al.,* "Implication of RNA Structure on Antisense Oligonucleotide Hybridization Kinetics," *Biochemistry* 31:12055-12061 (1992);
- Schmidt *et al.,* "The use of oligonucleotide probes containing 2'-deoxy-2'fluoronucleosides for regiospecific cleavage of RNA by RNaseH from Escherichia coli," *Biochimica et Biophysica Acta.* 1130:41-46 (1991); and
- Sigman *et al.,* "Chemical Nucleases," *Chem. Rev.* 93:2295 (1993).

The following references describe methods for characterizing nucleic acids. Some of these methods use enzymes, for example, to cleave nucleic acids for nucleic acid detection and/or characterization as well as describing basic research investigations into the mechanism of action of certain enzymes and proteins. Several of these references are not prior art, but are provided for thoroughness. Unlike the presently claimed invention, these references do not disclose methods of cleaving invasive cleavage structures or methods of detecting or characterizing nucleic acids based on the cleavage of invasive cleavage structures comprising nucleotide

analogs. Copies of all references except U.S. Patent No. 5,516,663 were provided in parent U.S. Patent Appln., Ser. No. 09/530, 309, now U.S Patent No. 6,348,314. A copy of U.S. Patent No. 5,516,663 is attached.

- U.S. Patent No. 5,882,867
- U.S. Patent No. 5,830,664
- U.S. Patent No. 5,792,614
- U.S. Patent No. 5,783,392
- U.S. Patent No. 5,516,663
- U.S. Patent No. 5,030,557
- PCT International Application No. WO 96/40999
- PCT International Application No. WO 95/14106
- PCT International Application No. WO 92/02638
- PCT International Application No. WO 89/09284
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- EP 0411186 A1
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- Higuchi, R., In Ehrlich, H.A. (Ed.), PCR Technology: Principles and Applications for DNA Amplification, Stockton Press, New York, pp. 61-70 (1991);
- Lee *et al.*, "Allelic discrimination by nick-translation PCR with fluorogenic probes," *Nucleic Acids Res.* 21(16):3761-3766 (1993);
- Li *et al.*, "Lagging Strand DNA Synthesis at the Eukaryotic Replication Fork Involves Binding and Stimulation of FEN-1 by Proliferating Cell Nuclear Antigen," *J. Biol. Chem.* 270:22109-22112 (1995);
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- Milligan and Ublenbeck, "Synthesis of Small RNAs Using T7 RNA Polymerase," *Methods Enzymol.* 180:51 (1989);

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- Smith *et al.*, "Novel Method of Detecting Single Base Substitutions in RNA Molecules by Differential Melting Behavior in Solution," *Genomics* 3:217-223 (1988);
- Uhlenbeck, "A small catalytic oligoribonucleotide," *Nature* 328:596-600 (1987); and
- Youil *et al.*, "Screening for Mutations by Enzyme Mismatch Cleavage with T4 Endonuclease VII," *Proc. Natl. Acad. Sci. USA* 92:87-91 (1995).

The following references, copies attached, describe oligonucleotides comprising modified bases or base analogs. Unlike the presently claimed invention, these references do not disclose methods of cleaving invasive cleavage structures or methods of detecting or characterizing nucleic acids based on the cleavage of invasive cleavage structures comprising nucleotide analogs.

- US Patent No. 6,140,496
- US Patent No. 6,037,120
- US Patent No. 6,001,983

The following references describe FEN-1 and other 5' nucleases, related proteins, polymerases, thermophilic organisms and their protein and nucleic acid sequences, as well as basic research investigations into the mechanism of action of certain endonucleases (*See e.g.*, Harrington and Murante references). Several of these references are not prior art, but are provided for thoroughness. Unlike the presently claimed invention, these references do not disclose methods for detecting target nucleic acids based on the cleavage of invasive cleavage structures comprising nucleotide analogs.

- U.S. Patent No. 5,874,283
- Bambara *et al.*, "Enzymes and Reactions at the Eukaryotic DNA Replication Fork," *J. Biol. Chem.* 272:4647-4650 (1997);
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- Harrington *et al.*, "The characterization of a mammalian DNA structure-specific endonuclease," *EMBO Journ.* 13:1235-1246 (1994);
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- Lieber, "The FEN-1 family of structure-specific nucleases in eukaryotic DNA replication,

recombination and repair," *BioEssays* 19:233-240 (1997);

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This Information Disclosure Statement under 37 C.F.R. §§ 1.56 and 1.97 is not to be construed as a representation that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

Dated: February 22, 2002

Mary Ann D. Brow
Registration No. 42,363

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
415/904-6500

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Attorney Docket No.: FORS-06910	Serial No.:
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Filing Date: Herewith	Group Art Unit:

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